
Women's Health: Cancer

Women and Breast Cancer

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Synopsis

One in every 12 women will develop breast cancer; the incidence increases with age, dietary fat intake,

caloric intake, height, and weight. The 10-year survival rate of breast cancer patients who refuse therapy is virtually zero. Segmental mastectomy plus radiation and lumpectomy, combined with systemic (adjuvant) chemotherapy, are alternatives under investigation at the National Institutes of Health that may increase the survival rate by decreasing metastatic complications.

BREAST CANCER IS an important health issue for women. It is a disease which is horrible in almost every sense, terrorizing because of its many extremely negative consequences, not only on survival, but on quality of life. However, substantial and worthwhile progress has recently been made, in our ability to diagnose the disease, to treat this disease while it remains localized to the breast, and to improve survival.

Many women, correctly in some sense, are terrorized by the fear of breast cancer, not only because of what it means to them with respect to survival, but also because of its major impact on lifestyle, self-image, sexuality, and how they see themselves.

This view of breast cancer has been slow to change because progress has been slow. I think it might be plausible for us to begin to bury such an image of breast cancer as we turn to new, less mutilating, and more effective modalities of treating this disease.

Breast cancer is still the most common serious malignancy of women in terms of incidence and therefore in terms of its local management as a problem confined to the breast. One woman in approximately 12 will develop breast cancer in her lifetime. At present, the incidence rates for breast cancer are not changing dramatically, although there are potential interventions that have already been mentioned which might reduce breast cancer incidence.

Incidence rates for breast cancer as a function of age continuously rise in North America throughout a woman's life. About two-thirds to three-quarters of the cases of breast cancer involve women who are over the age of 50 or approximately postmenopausal,

but one-quarter to one-third of breast cancer occurs in women who are under 50.

When the annual incidence rate for women in other parts of the world is compared with that of North American women, women from the Orient, for example Japan, have an extraordinarily lower incidence of breast cancer, particularly in that period in a woman's life when breast cancer is most common, after the age of 60. The incidence rate in Japan of approximately 40 per 100,000 is remarkably lower compared with approximately 400 per 100,000 for women over the age of 80 in North America.

There is not time to review the evidence that explains some of these differences, but it is agreed that these are not intrinsic or genetic differences between Oriental women and women living in North America. These differences are almost completely environmentally determined; they reflect the differences in environment and lifestyle between Oriental women and women in North America. The data strongly suggest that these are nutritionally regulated factors, in part due to intake of dietary fat, and even more importantly to total intake of calories. Body size, height, and weight are extraordinary risk factors for breast cancer.

While I agree that telling a woman to stop eating is trite and an overly easy thing to say to anybody who is trying to lose weight, it nonetheless is true that nutritional issues can have an enormous impact on breast cancer incidence, and ongoing trials aimed at exploring the usefulness of dietary interventions are under way. There is convincing information to suggest that such measures taken by a large number of women would greatly reduce their risk of breast and colon neoplasms.

'... we believe very strongly that women should be encouraged to participate in clinical trials to improve their own health. Less than 2 percent of women developing breast cancer in the United States participate in clinical trials.'

When one talks about what progress has been made in treating breast cancer, it is worth mentioning what the results are for not treating breast cancer. There have been women who, for various reasons, have refused any kind of therapy for their breast cancer. Women who take no therapy when they develop breast cancer die of the disease within 5 to 10 years. So that the baseline situation is that untreated breast cancer is almost invariably fatal.

Superimposed on this notion that untreated breast cancer was a fatal disease was the development pioneered by Halsted, who introduced an operation in which the breast was resected and all of the tissue in the region around the breast was removed. Halsted envisioned that breast cancer spread the way ripples might spread from a rock thrown into a pond, and therefore by doing a radical operation in which he attempted to draw a bigger circle around these spreading ripples, he hoped to cure patients with breast cancer.

There is no question that this is a mutilating operation, but it was an operation that was proposed on a scientific basis and, in fact, was a successful operation. We need to not lose sight of that. Compared to the studies on untreated breast cancer, where survival at 10 years was in the 5 percent or less range, with the introduction of this radical surgery, there was a dramatic improvement in survival rate over the years, so that one may conclude that in some women with breast cancer, the disease is localized to the breast, and an operation of this sort can save their lives. However, because of the nature of the operation, and because it became clear that breast cancer did not just spread as ripples from a rock thrown into a pond, it was worth exploring the less radical means of treating breast cancer.

Leaders in this field have been researchers in the National Surgical Adjuvant Breast Project. They recently reported a trial in which women with breast cancer that was apparently localized to the breast and regional lymph nodes under the arm—we call these patients stage one and stage two—were prospectively randomized to three different protocols: a

modified radical mastectomy; an operation in which a wide excision, not really a lumpectomy, but a wide excision of the tumor, was performed and lymph nodes under the arm were also removed; or this same operation plus breast irradiation. Although the women have not been followed for long periods of time as yet, and there are some objections to this trial, the survival of the women who had the less radical surgery is no worse than that of women who have had a mastectomy. This has led people to believe that mastectomy need not be necessary for many women with breast cancer.

However, the procedures used in this study involved a substantial degree of breast surgery, and many of us wondered whether it might be possible to perform a breast conservative procedure, i.e., just removing the tumor, leaving the breast, and attempting to control the disease in the breast by radiotherapy. Here at the National Cancer Institute (NCI), together with several of my colleagues, we have been conducting a study on women who have given us an informed consent and who have apparent localized breast cancer (stage one or stage two). We randomized these women to receive either a simple mastectomy plus removal of the lymph nodes or a lumpectomy, the removal of the tumor plus removal of the lymph nodes, and irradiation of the region. Our goal in this ongoing trial is to conclusively determine whether women treated with less than a mastectomy, a nonmutilating kind of procedure, can have equivalent or even superior survival to women managed with mastectomy.

Local control of the disease and adequate reconstruction for women who have had a mastectomy is a major achievement that has occurred in the last decade. However, even for a woman who practices excellent breast self-examination, even for a woman who reports regularly for mammography, it is likely that the tumor has existed in her body for 2, 3, perhaps even 5 years prior to when it can be detected.

You need to appreciate that breast surgery or breast irradiation is like a spotlight. It is treatment aimed at one spot in a woman's body, and breast cancer cells, which have escaped from the primary tumors and spread through the bloodstream and have formed new deposits or metastases elsewhere in a woman's body, cannot possibly be treated by any therapy that is aimed directly at the breast. This is the definition of systemic breast cancer, and this is the aspect of the disease which results in nearly 40,000 deaths a year in the United States.

The tumor in the breast can, by its ability to invade through blood vessels, spread through the bloodstream to other parts of the body. The reason we

remove lymph nodes under the arm and why we recommend that this procedure be done for all women who have cancer breast, is because we know that involvement of these lymph nodes by tumor cells is like a footprint. It is the equivalent of saying that if there are breast cancer cells here, there is a strong, statistical likelihood that there will be other microscopic, undetectable deposits of breast cancer elsewhere in bone or lung or wherever that may grow and lead to metastatic disease, which will eventually be fatal.

And with this goal in mind, many groups of investigators have asked whether women who, at the time of either lumpectomy or mastectomy have involvement of their lymph nodes and therefore are at increased risk of developing metastatic disease, should be treated prophylactically with something that we call adjuvant therapy, a systemic drug or hormone treatment which might improve their survival. This kind of systemic approach has resulted in a substantial and significant improvement in survival of women with breast cancer and is one of the most significant advances in cancer treatment that we have ever had the good fortune to support.

This therapy has side effects. Women have every reason to be concerned about how they will feel, what they will look like while they are getting this treatment, and potential long-term side effects. However, if we considered every trial in the world in which chemotherapeutic drugs were administered to women with breast cancer, whether they had lymph node involvement or not, there was at least a 30 percent reduction in their relapse rate as a result of receiving this chemotherapy. This is a substantial benefit.

Furthermore, Hyrniuk has looked at the ability to remain free of disease as a function of how aggressively this therapy was given to women. There is an extremely significant relationship between giving this therapy aggressively for a short period of time and improvement in relapse-free survival. Thus, we already have the means at hand to make this therapy more effective, without even requiring some hoped-for, nontoxic breakthrough in the future.

Even for women who have no lymph node involvement, Gianni Bonadonna has shown that the use of a three-drug combination for 6 months compared with a control group of women who did not receive this therapy produced a dramatic improvement in overall survival. These are exciting data, and they suggest a major impact on treatment for women with breast cancer.

These therapies are toxic, and we would all like to have nontoxic treatments for breast cancer. All of you appreciate that normal breast tissue responds to

female sex hormones. Without estrogens, breasts would not develop at puberty. Breast cancer remembers this property some of the time, and therefore, it is reasonable to attempt to treat breast cancer prophylactically with therapies that reduce hormone concentrations or antagonize their action; we call these drugs anti-estrogens, and in one study, women who received an almost completely nontoxic pill, called tamoxifen, had a substantial improvement in survival compared with women receiving a placebo. And if one once again looks at every study that has examined this question there is, for women over 50, nearly a 20 percent improvement in survival (reduction in mortality), as a result of receiving this essentially nontoxic therapy.

In September 1985, we convened a meeting at NCI to review this information on breast cancer in women, and these were the results. First of all, we believe very strongly that women should be encouraged to participate in clinical trials to improve their own health.

Less than 2 percent of women developing breast cancer in the United States participate in clinical trials. Frequently, as is the case, for example, here at the Clinical Center, all medical costs are free to patients who are treated in such trials, and there are many other advantages to participation at major academic centers, and yet many women never find out about such trials and are not informed about them.

Chemotherapy is indicated and will dramatically improve survival for young women with positive lymph nodes. Chemotherapy should also be considered for certain women who are lymph node negative and who are under 50. There are major benefits for these women. For women who are over 50, the anti-estrogen tamoxifen is clearly associated with an improvement in survival, and the consensus panel concluded that chemotherapy should be considered for women who are over 50 and who have lymph node involvement with breast cancer. I personally think that this was too conservative a recommendation and that the data are clear that this therapy can be lifesaving for women over 50 as well, and finally that chemotherapy might be considered for node-negative women who are over 50.

So this is a very exciting time in the management of breast cancer. I do not think that we need to see as many women succumb to this disease nor as many women mutilated. To some extent, this is an issue involving more women participating in such trials, and to some extent this is simply a matter of women receiving those therapies which are already proven, to lessen both the impact of the disease locally and to increase their chances of survival.